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# FATIGUE AND THE EXPERIMENTAL PATHOLOGY OF THE HEART

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The history of research into the processes of fatigue and recovery is a striking example of the fruitfulness of the major directions followed by physiology in our country, and of the importance of correct views on methodology in the solution of problems of physiology.

Even in the period when metaphysical "theories" of fatigue -- exhaustion, oppression, revulsion, etc -- had the field to themselves abroad, the work of our scientists was characterized by orderly physiological analysis and synthesis in the study of fatigue as a complex, complicated and integrated phenomenon.

A decisive influence on the study of the processes of fatigue was exercised by the founders of physiology in our country -- I. M. Sechenov, I. P. Pavlov, and N. E. Vvedenskiy.

Even in one of his early works, "Nitrogen Balance in the Submaxillary Salivary Gland During Work," Pavlov indicated with particular force the interrelation between the processes of fatigue and recovery.

If experimental studies of fatigue are now very numerous, and the manifestations of fatigue well known, the nature and specifics of the processes of recovery have nevertheless not attracted the attention of researchers they should have.

The thoughts and concepts of I. P. Pavlov on the interrelation between the processes of fatigue, recovery, and inhibition were subsequently further elaborated and experimentally developed in the work of G. V. Fol'bort and his associates.

The basic method used in Fol'bort's work is the study of changes in the work capacity (efficiency) of organs as the result of the dynamic interrelation of the processes of fatigue and recovery. This concept of change in the functional capacity of an organ as the result of the unity and struggle between opposing processes represents application of the dialectical method to the study of natural phenomena.

As the normal functioning of an organ is based on a specific interrelation among physiological processes, it follows, in accordance with the views of I. P. Pavlov, that any significant disturbance in these relations may result in the development of a pathological condition. Activity of extraordinary intensity, and pronounced predominance of fatigue over the processes of recovery, may result in functional insufficiency and pathological change.

From this it is clear that elaboration of the problems of interrelation between the processes of fatigue and recovery lead in the direction of the discovery of the mechanisms and causes of the development of functional insufficiency, and, consequently, to the elimination thereof. Seen from this angle, G. V. Fol'bort's concept takes on significance for general pathology and practical medicine.

The role of changes in the interrelation between fatigue and recovery in the development of pathological changes emerges

with particular clarity when applied to the functioning of the heart.

Cardiac muscle fatigue finds its origin in a variety of factors. It may develop as the result of a marked rise of long duration in resistance to the flow of blood ejected by the heart, of marked increase of long duration in diastolic filling, or marked tachycardia of long duration.

Many ascribe the development of compensatory mechanisms in cardiac fatigue solely to changes in the pulse volume, in connection with cardiac filling. By Starling's "law of the heart," we know that the energy set free at each contraction is proportional to the length of the heart's fibers before contraction, i.e., to the degree of diastolic expansion. Rossler and Unna, employing cardio-pulmonary matter to study change in cardiac cavity elasticity and pressure with the pericardium closed and open, believe that the pericardium restricts expansion of the heart, and specifically of the right auricle.

According to Starling, increased filling requires the fatigued heart to expand considerably more than usual to increase the pulse volume.

The "law of the heart" is also widely employed by clinicians to explain its adaptive reactions in fatigue.

It is necessary to point to the fact that Starling's "law of the heart" has but exceedingly relative validity both in the normal state and in pathology. It is not mechanical peculiarities of the filling of the heart, but the intensity of trophic processes,

the interrelation between fatigue and recovery, and reflex effects which determine the state of the contractive capacity of the myocardium at a given moment.

This is attested by the experiments of I. P. Pavlov in investigating the effect of the accelerating nerve on the heart. Contractions were observed to increase without change in rhythm, the volume of the heart declining. Nikolayev holds that cardiac glucosides strengthen and shorten the systole, while the volume of the heart decreases. Kurshakov and Ratner have noted a shortening of the diastole in cardiac fatigue.

Our experiments testify to the fact that the level at which trophic processes proceed -- the interrelation between fatigue and recovery -- is the decisive factor in changing the contractile capacity of the myocardium, rather than filling.

We have demonstrated in experiments with the arrested hearts of rabbits and frogs that the level of contraction declines sharply in significant diastolic filling when rhythm is very slow. Identical results have been obtained in experiments with isolated strips from the ventricles of rabbits and frogs. Here the factor of diastolic filling is completely eliminated.

Reduction in the magnitude of cardiac contraction when the rhythm has been markedly slowed may be explained in terms of the concepts of G. V. Fol'bort. Activity and developing fatigue are the major stimuli of the processes of recovery. A marked slowing in the rhythm of the heart, weakening its activity, results in reduction of the intensity of the processes of recuperation. This low is supported by the fact that any marked slowing of the rhyth...

of cardiac contractions after fatigue leads not to decline, but to elevation of the degree of cardiac contraction. In the given instance, elevation of the cardiac contractions is a result of the intensity of the recuperative processes, stimulated by prior fatigue.

Thus, in the case of significant diastolic filling and the weakening of the intensity of recuperative processes we witness a decline in the strength of the contractions.

The experimental findings set forth above have this further significance in principle. In clinical and experimental work, cases of contractile myocardial insufficiency due to fatigue are well known. We have submitted instances of declining cardiac contractile capacity as a result of the weakening of the recuperative processes.

It is our belief that insufficiency in the contractile capacity of the myocardium due to weakening in the intensity of the restorative processes is not merely an experimental condition, but may be encountered in clinical work.

Training, and the application of load on the cardiovascular system in fixed doses, constitute factors sustaining a fixed degree of intensity in the restorative processes within the heart, this in turn making the heart more resistant to the demands placed upon it in the presence of both normal and pathological states.

Study of the interrelation between the processes of fatigue and recovery enabled G. V. Fol'bort to orient himself in the mechanism of the development of training and chronic exhaustion. Training (adaptation) occurs only when a new load is applied to

an organ that had recovered its functional state before this application. If exhausting activity be repeated before the attainment of complete recuperation, chronic exhaustion may result.

From the viewpoint of the concepts adduced above, the mechanism of development of hypertrophy may be understood as the reaction of the myocardium in response to intensive activity of long duration. At a given stage the development of hypertrophy of the cardiac muscle is an example of intensification of the restorative processes resulting in morphological changes.

Rich experimental data has demonstrated the development of hypertrophy of the cardiac muscle under various conditions requiring intensive cardiac activity which stimulates restorative processes.

Zasetskiy has reported hypertrophy in cats doing intensive work over a long period of time. Timofeyev has observed experimental hypertrophy of the cardiac muscle, producing aortal insufficiency in dogs. Eisler has reported hypertrophy as a result of the narrowing of the aorta in dogs. Drury and Wightman have produced hypertrophy (primarily of the auricle) by creating resistance through anastomoses of the right carotid artery with the right jugular vein.

The compensatory significance of cardiac hypertrophy, serving to overcome existent obstacles in the circulatory system, continues for a specific period of time. Maintenance of a load of unchanging intensity changes the relationship between the processes of exhaustion and restoration, and leads to chronic exhaustion and weakening of cardiac activity. The possibility of exhausting the hypertrophied heart has been demonstrated experimentally

by Dobroklonskiy, Timofeyev, Duhring, Ritand and Dock, Edsall, Hunt and Reed, et al.

The development of exhaustion of cardiac muscle, and reduction of the contractile capacity of the myocardium often constitutes the terminal phase in the clinical picture in many pathological processes in the circulatory system. The significance of cardiac insufficiency has been repeatedly emphasized by such prominent Soviet clinicians as Lang and Strazhesko.

We have posed the question of the role of fatigue in producing disturbances in the automatism and conductivity of cardiac muscle. It is only recently that fatigue has gained the attention of researchers and clinicians as a state leading to disturbances in these myocardiac functions.

Current thinking (Smirnov) holds the heart to be a nonuniformly excited system. The lack of uniformity of the departments of the heart -- the auricular muscles, the ventricles, the system of innervation -- is expressed in their varying excitability, impulse conductivity, and capacity to function automatically. In considering the effect of load applied to any portion of the heart, the localization of fatigue will be determined to a considerable degree by the functional lability of the various portions of the cardiac muscle.

Our first data on the effect of fatigue on the automatic functioning of the heart was obtained in studies of cardiac fatigue during investigation of heterotopic automatism in complete atrioventricular block. In an experiment with frogs, atrioventricular block was attained by Stannius' ligature, while with

rabbits is established by injection of chloralhydrate into the base of the interauricular diaphragm.

The first manifestation of the onset of fatigue in the cardiac ventricles, functioning on the basis of automatic atrioventricular action, is disturbance in rhythm against a background of progressive reduction in the frequency of cardiac contractions, bradyarrythmia. In profound fatigue, the pacemaker functions intermittently. Removal of the load borne by the heart leads to restoration of the initial frequency of ventricular rhythm. The rapidity with which the normal rhythm of ventricular contraction is restored is determined by the depth and speed with which the prior fatigue has developed. In other words, we see in the change of the function of automatism a demonstration of the general principles governing the interrelation between the processes of fatigue and restoration.

The special features of change in atrioventricular rhythm which we have described -- irregular retardation and periodic activity -- are apparently common to other organs with automatic functions. We know, for example, of uneven slowing, and intermittent function, in the respiratory center and the ureter, under unfavorable conditions.

Clinicians adduce instances in which the onset of marked retardation in atrioventricular rhythm when complete block is definitely established leads to cardiac syncope of the Adams-Stokes type (Bol'skiy, Strazhesko, Lewis, Davydov, Mackenzie, Kolonin, etc). The character of the disturbance in rhythm and the conditions under which it arises are exceedingly similar to the changes we have described.

The experiments we have adduced represent an experimental model of the clinical cases of disturbances in atrioventricular rhythm that have been described, in which exhaustion of cardiac muscle plays a role of no little importance.

Fatigue of cardiac structures involved in the automatic operation of the heart may also occur under relatively isolated conditions. We have demonstrated this in changes in the function of atrioventricular automatism at the moment of institution of complete block. It is common knowledge that the moment at which a complete atrioventricular block is established is the most dangerous to the life of the patient. The duration of stoppage of ventricular function depends upon the operation of the atrioventricular automatic control. At the moment under consideration, the atrioventricular node emerges from the state produced by the effect of the excitatory impulses from the sinus node. A frequent rhythm of excitation from the sinus node may result in fatigue in the atrioventricular node, which would manifest itself in bradyarrythmia at the moment when complete block sets in. In this situation exhaustion of the function of automatic control sets in while the myocardium still exercises its normal contractile capacity.

Vvedenskiy proposed a new concept and provided a concrete characterization on the basis of which it is possible to evaluate the manner and direction of change in the current functional state of an organ: its lability. According to Vvedenskiy, lability is determined by the number of excitations reproduced by tissue in unit time. We have demonstrated experimentally that functional lability in fatigue changes to different degrees in different portions of the heart, that of the atrioventricular node showing

greatest decline. Insofar as the conductivity of impulses between the auricles and the ventricles is governed by the atrioventricular node, it is understandable that in exhaustion of the cardiac muscle as a result of reduction in the lability of the atrioventricular node we were witness to the phenomenon of incomplete block. Chernogorov, Puymer, and others hold that atrioventricular block is parabiotic in nature. It is apparent that fatigue, reducing the lability of the node, facilitates the development of parabiotic inhibition therein.

Instances of reduction in the lability of the atrioventricular node due to fatigue have been observed in clinical practice.

It is common knowledge that disturbance in hemodynamics in cardiac insufficiency is the cause of complex circulatory disorders.

In another series of experiments we have shown that cardiac fatigue produces reflex effects in its interoreceptors, which change the functional condition of the spinal cord and the respiratory center. Thus, the processes of fatigue and recovery may serve as stimuli of the receptor apparatus of the heart, and may affect the activity of other organs by reflex action.

Clearly, the study of cardiac reflexes in cardiac insufficiency can contribute much to the understanding of the mechanisms of circulatory disturbance.

Further experimental study of cardiac exhaustion is one of the paths to be followed in creating new model concepts of pathological states in the circulatory system.